Pulmonary Embolism

- Pulmonary embolism occurs when the proximal portion of the clot breaks off, travels through the veins, transverses the right ventricle and lodges in precapillary pulmonary artery.
- They can be from popliteal, common femoral, superficial femoral, pelvic axillary jugular veins.

People at Risk for Thromboembolism
Surgery : Major surgery abdominal, gynecologic , urologic, orthopedic, neurosurgery, cancer related surgery.
Trauma : Multisystem trauma, spinal cord injury, spinal fracture, fractures of hip and pelvis.
Malignancy :Any malignancy, overt to covert Risk is higher during chemotherapy & radiotherapy.
Acute medical illness :Stroke, acute myocardial infraction, heart failure, neuromuscular weakness syndromes
Patient specific factors:Histroy of thromboembolism, obesity, increasing age more than 40yrs, hypercoagulable state.
ICU related factors: Prolonged mechanical ventilation, neuromuscluar paralysis, central venous catheter, severe sepsis, consumptive coagulopathy, heparin induced thrombocyopenia.
Pregnancy

CLINICAL FEATURES

- Dyspnea unexplained by auscultatory findings.
- Chest pain with pleuritic features
- PE can cause infarct in the basilar lung segment can manifest as referred pain to shoulder & may mimic biliary or ureteral colic.
- In addition to pain & dyspnea approx 5 to 8% of patients with PE in the ED present with near or full syncope, or new onset confusion probably due to impaired cardiac output causing cerebral hypoxia.

- Tachypnea, tachycardia, low pulse oximetry reading

Pretest Probability

WELLS SCORE FOR PE	
Suspected DVT	3
Alternative diagnosis less likely than PE	3
HR>100bpm	1.5
Prior DVT	1.5
Immobilization within prior 4wks	1.5
Active malignancy	1
Hemoptysis	1

>6 Points high risk; 2-6 moderate risk; <2: low risk.

Pulmonary embolism rule out criteria (PERC rule)

- Age <50yrs
- Pulse oximetry >94%
- HR<100 bpm
- No prior venous thromboembolism
- No recent surgery or trauma
- No hemoptysis
- No estrogen use
- No unilateral leg swelling

- Any item present PERC is positive.
- Studies have suggested safe exclusion of PE in patients with low clinical probability who, in addition,met all criteria of the PERC rule.

Geneva Original and Simplified Version

Items	Clinical decision rule points	
	Original version[91]	Simplified version[87]
Previous PE or DVT	3	1
Heart rate		
75–94 b.p.m.	3	1
≥95 b.p.m.	5	2
Surgery or fracture within the past month	2	1
Haemoptysis	2	1
Active cancer	2	1
Unilateral lower-limb pain	3	1
Pain on lower-limb deep venous palpation and unilateral oedema	4	1
Age >65 years	1	1
Clinical probability		
Three-level score		
Low	0–3	0–1
Intermediate	4–10	2–4
High	≥11	≥5
Two-level score		
PE-unlikely	0–5	0–2
PE-likely	≥6	≥3

DIAGNOSIS

D-DIMER

- Produced due to plasmins breakdown of fibrin.
- In 95% of patients with no PE the levels <500ng/ml
- Half life of D-Dimer is 8 days.
- It may remain elevated upto 3 days after a symptomatic VTE.

- Use of age adjusted cut-offs may improve the performance of D-dimer testing in the elderly. Age adjusted cut-off (age 10mg/L, for patients aged>50 years.
- It is not specific ; may be elevated in MI, sepsis, pneumonia, cancer, 2 or 3rd trimester

ELEVATED BIOMARKERS

- Serum troponin may be elevated due to RV infraction
- BNP may be elevated due to stretching of RV.

X ray :

- Cardiomegaly, basilar infiltrates or pleural effusion
- inWestermark sign: Wedge shaped area of lung oligemia due complete lobar artery obstruction
- Hampton hump: Peripheral dome shaped dense opacification.

ECG :

- Sinus tachycardia, non specific ST-T changes
- Complete or incomplete right bundle branch block
- S1Q3T3 (Mc Ginn white sign)

CT Angiogram

- Multidetector CTPA is the method of choice for imaging the pulmonary vasculature in patients with suspected PE.
- PIOPED II study observed a sensitivity of 83% and a specificity of 96% for CTPA in PE diagnosis.

Ventilation perfusion scan

- Lung scanning is a second line diagnostic test for PE .
- V/Q lung scanning can identify a perfusion defect when ventilation is normal.
- A V/Q scan that demonstrates two or more apex central wedge shaped defects in perfusion then the probability of PE is >80%.

Venous US

- Has a diagnostic sensitivity of 90-95% & specificity of 95% for DVT.
- They operate on the principle that normal vein is compressible whereas a thrombosed vein is not.

ECHO

- It is used to stratify early risk of patients with PE.
- RV/LV diameter ratio >1 and TAPSE <16mm are the findings for which an association with unfavorable prognosis.
- To rule out MI, Pericardial tamponade, aortic dissection.

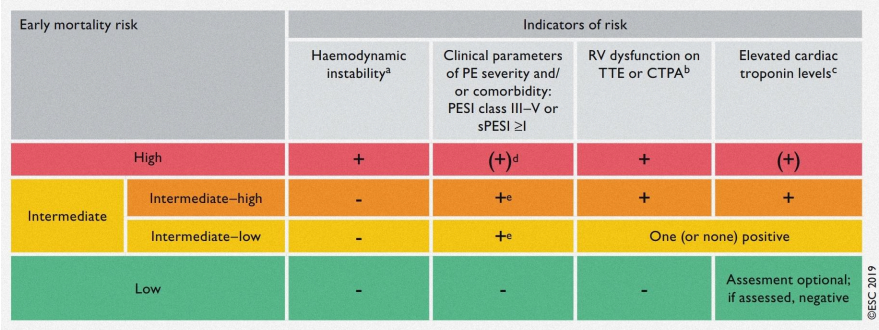
Risk Stratification

- The PESI in it's original or simplified form is the most extensively validated and most broadly used clinical score to date,as it integrates baseline indicators of the severity of the acute PE episode with aggravating conditions and the comorbidity of the patient. Overall,a PESI of classI- II or an sPESI of0 is a reliable predictor of low-riskPE.

Parameter	Original version[226]	Simplified version[229]
Age	Age in years	1 point (if age >80 years)
Male sex	+10 points	–
Cancer	+30 points	1 point
Chronic heart failure	+10 points	1 point
Chronic pulmonary disease	+10 points	
Pulse rate ≥110 b.p.m.	+20 points	1 point
Systolic BP <100 mmHg	+30 points	1 point
Respiratory rate >30 breaths per min	+20 points	–
Temperature <36°C	+20 points	–
Altered mental status	+60 points	–
Arterial oxyhaemoglobin saturation <90%	+20 points	1 point
	Risk strata[a]	
	Class I: ≤65 points very low 30 day mortality risk (0–1.6%) **Class II: 66–85 points** low mortality risk (1.7–3.5%)	**0 points =** 30 day mortality risk 1.0% (95% CI 0.0–2.1%)
	Class III: 86–105 points moderate mortality risk (3.2–7.1%) **Class IV: 106–125 points** high mortality risk (4.0–11.4%) **Class V: >125 points** very high mortality risk (10.0–24.5%)	**≥1 point(s) =** 30 day mortality risk 10.9% (95% CI 8.5–13.2%)

Treatment of PE

Management of PE depends on risk stratification of the patient.



Early mortality risk		Indicators of risk			
		Haemodynamic instability[a]	Clinical parameters of PE severity and/or comorbidity: PESI class III–V or sPESI ≥I	RV dysfunction on TTE or CTPA[b]	Elevated cardiac troponin levels[c]
High		+	(+)[d]	+	(+)
Intermediate	Intermediate–high	-	+[e]	+	+
	Intermediate–low	-	+[e]	One (or none) positive	
Low		-	-	-	Assesment optional; if assessed, negative

- Patients with high or intermediate clinical probability should receive anticoagulation even while the results are awaited.

Low molecular weight heparin

- LMWH and fondaparinux are preferred over UFH for initial anticoagulation in PE, as they carry a lower risk of inducing major bleeding and heparin-induced thrombocytopenia

- DOSE : Enoxaparin 1mg/kg by SC every 12h.
- LMWH is cleared by kidneys and dose adjustments are necessary in pts with renal impairment. In renal failure UFH is recommended over LMWH.

Monitoring

- The aPTT can be used to monitor anticoagulation with UFH heparin because it primarily reflects activity of factor IIa.
- aPTT cannot be used to monitor anticoagulation with LMWH because they act primarily on factor Xa. Usually it is not necessary to monitor but if needed then Factor Xa should be measured.

Heparin

- It is recommended for patients with serious renal impairment CrCL< 30ml/min.
- The standard treatment of both deep vein thrombosis and acute pulmonary embolism is UFH given by continuous IV infusion .
- Prepare heparin infusion by adding 20,000 IU heparin to 500ml diluent.
- Give an initial bolus dose of 80IU/kg & follow with continuous infusion of 18 IU/kg/hr.
- Check aPTT after 6hrs and adjust heparin dose as below

aPTT	aPTT Ratio	Bolus dose	Continuous infusion
<35	<1.2	80IU/Kg	Increase by 4 IU/kg/hr
35-45	1.2 -1.5	40 IU/kg	Increase by 2 IU/kg/hr
46 – 70	1.5 – 2.3	-	-
71-90	2.3-3.0	-	Decrease by 2 IU/kg/hr
>90	>3.0		Stop infusion for 1hr then decrease by 3 IU/kg/hr

Fixed dose regimen : Fixed subcutaneous dosing : 333 U/kg as a first dose, then 250 U/kg twice daily.

Novel Anticoagulants

- NOACs are small molecules that directly inhibit one activated coagulation factor, which is thrombin for dabigatran and factor Xa for apixaban, edoxaban, and rivaroxaban.
- They have predictable bioavailability and therefore can be given at fixed dose without monitoring.

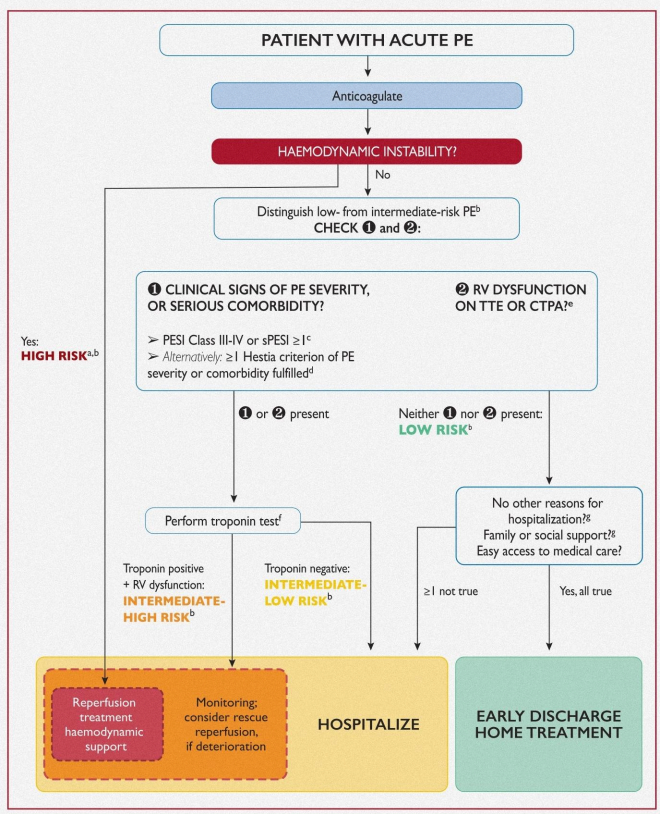
Drug	Treatment Dosage	Half Life
Rivoraxaban	15 mg twice daily for 3 weeks, then 20 mg orally once daily.	7 – 11 hrs
Apixaban	10mg BD for 7 days then 5mg BD	
Dabigatran	150 mg orally BD after 7 -10 days of LMWH	14 – 17 hrs
Fondaparinux	Weight < 50 kg : 5 mg SC every 24 hrs Weight 50 – 100 kg :7.5 mg SC every 24 hrs Weight > 100kg : 10mg SC every 24 hrs	17 -21 hrs
Unfractionated Heparin	Weight based bolus followed by weight based infusion adjusted to maintain therapeutic activated partial thromboplastin time or anti X level. Fixed SC : 333 U/kg as 1st dose, then 250U/kg twice daily.	1.5 hrs
Warfarin	Dose : 0.5 -6 mg/day orally Adjust the dose to maintain INR 2 - 3	36hrs

Vitamin K Antagonist

- Once systemic anticoagulation is initiated and after initiation of parenteral therapy VKA's can be started.
- Vitamin K antagonist prevents carboxylation activation of coagulation factor VII,IX,X,XI
- Full effect needs atleast 5 days.
- If it is initiated as monotherapy during an acute thrombotic illness a paradoxical exacerbation of hypercoagulability can increase the likelihood of thrombosis rather than preventing.
- UFH/LMWH/Fondaparinux is initiated along with warfarin for atleast 5 days & until two sequential INR values at least 1 day apart, achieves target INR (2.0 -3.0).
- Dose 5mg OD ; 7.5 or 10mg is used in obese individuals.

Duration of Anticoagulation Therapy

- Patients with VTE due to transient risk factors like surgery require only 3 months of anticoagulation as it is associated with a very low thrombotic recurrence risk after adequate treatment.
- Patients have a first VTE following a non surgical events such as pregnancy, major trauma or significant immobilization after medical illness, they have an intermediate risk of recurrent VTE. Despite high risk, 3 months of anticoagulation is enough.
- Patients presenting with second unprovoked VTE have to receive anticoagulation for 3 -6 months.
- Indefinite treatment is recommended for un unprovoked VTE, active cancer, APLA.



Thrombolytic therapy

- Thrombolytic agents may accelerate thrombolysis by activating plasminogen to form plasmin resulting in fibrinolysis as well as fibrinogenolysis.
- Thrombolysis leads to early patency of an occluded vein but it does not decrease the rate of PE.
- Meta-analysis suggests that it may decrease post thrombotic syndrome but at the expense of an increase in major bleeding, it has also not demonstrated to reduce the rate of recurrence, PE or death.The mortality benefit by thrombolysis is still not evident. Hence the decision to thrombolysis should be based on a case by case scenario .

- It is reserved only for life threatening cases; only for massive pulmonary embolism.
- Massive pulmonary embolism is a PE with SBP < 90mmHg or SBP <100 mmHg in a hypertensive patients or a 40% reduction in baseline systolic BP.

- Alteplase : 100mg IV infused over 2hrs. (FDA Approved agent).
- Streptokinase 2,50,000 U IV loading dose during 30 min; then 1,00,000 U/h for 24h
- Reteplase 10U by bolus and repeat in 30min; currently not approved to be used in PE.
- Tenecteplase dose is 0.5mg/kg IV bolus.

Molecule	Regimen	Contraindications to fibrinolysis
rtPA	100 mg over 2 h	**Absolute**
	0.6 mg/kg over 15 min (maximum dose 50 mg)[a]	History of haemorrhagic stroke or stroke of unknown origin
Streptokinase	250 000 IU as a loading dose over 30 min, followed by 100 000 IU/h over 12–24 h	Ischaemic stroke in previous 6 months
	Accelerated regimen: 1.5 million IU over 2 h	Central nervous system neoplasm
Urokinase	4400 IU/kg as a loading dose over 10 min, followed by 4400 IU/kg/h over 12–24 h	Major trauma, surgery, or head injury in previous 3 weeks
	Accelerated regimen: 3 million IU over 2 h	Bleeding diathesis
		Active bleeding
		Relative
		Transient ischaemic attack in previous 6 months
		Oral anticoagulation
		Pregnancy or first post-partum week
		Non-compressible puncture sites
		Traumatic resuscitation
		Refractory hypertension (systolic BP >180 mmHg)
		Advanced liver disease
		Infective endocarditis
		Active peptic ulcer

Contraindication

- Absolute : Previous hemorrhagic stroke, Intracranial surgery or trauma, active internal bleeding.
- Relative : Bleeding diathesis, thrombocytopenia, recent major trauma, internal bleeding or non hemorrhagic stroke, uncontrolled severe hypertension, cardiopulmonary resuscitation, recent major surgery, pregnancy.

Catheter Directed Thrombolysis v/s Standard Therapy

- Thrombolytic associated reductions in PTS were seen in a recent randomized trial comparing catheter-directed thrombolysis with standard therapy for iliofemoral DVT.
- Thrombolytic therapy almost doubled vein patency at 6 months (66% vs 47%) and was associated with significantly less PTS at 24 months (41% vs 56%).
- Thrombolysis was associated with more bleeding complications and did not prevent recurrent events and mortality was no different in the 2 groups.
- At present evidence is inadequate for recommendation.
- Catheter directed lysis may be useful in patients with : iliofemoral DVT, symptoms less than 14 days, good functional status , life expectancy greater than 1 year and low risk of bleeding.

Inferior venacava filters

- Retrievable or permanent inferior vena cava filters may be used when there is contraindication to anticoagulation therapy for patients with newly diagnosed proximal DVT or PE.
- Mesh like filters are kept in inferior venacava to trap thrombi that break loose from leg vein and prevent them from traveling further.
- One risk is development of thrombosis at the filter itself. A standard dose of anticogulation should be administrated if contraindication resolve.

Pulmonary Embolectomy

- Surgical embolectomy is a last resort, can be done select group of patients with documented central PE and refractory cardiogenic shock despite maximal therapy.

● **Malignancy & VTE** ● ● Long term anticoagulation with LMWH instead of warfarin appears to be more effective at preventing recurrent venous thrombosis without a statistically increase in bleeding risk. ● All the patients should be treated for atleast 6 months.

PERIPARTUM PE

During pregnancy all elements of virchows triad is present

- Hypercoagulability
- Venous stasis
- Venous trauma

Venous statsis : Compression of the pelvic veins by the gravid uterus, compression of left illiac veins by illiac artery.

Venous trauma: Pulsatile compression of left common illiac vein leads to endothelial damage & predispose to thrombus formation.

Hypercoagulability:

- Significant increase in levels of factor V, IX, X, VIII,
- Decrease in protein S.
- Increase in protein C resistance, Plasminogen activator inhibitor, Thrombin activated fibrinolysis inhibitor.

Anticoagulation strategy for labour & delivery

- LMWH can be administrated safely and is now the treatment of choice. Twice daily treatment is preferred over OD dosage.
- VKA should not be used during pregnancy because of their teratogenic effects in the first trimester of pregnancy.
- If an acute DVT or PE occurs close to delivery, interrupting anticoagulation may be hazardous because of high risk of PE. IVC filter should be considered in such cases.

On	● Switch to UFH 10,000 U twice a day at 36

prophylactic dose of LMWH for remote clot	wks of gestation ● Discontinue UFH 12h before procedure
Patient is on therapeutic dose of LMWH (VTE > 1mnth)	● Switch to UFH at 36wks of gestation. ● Discontinue 12-24h before procedure. ● Restart IV UFH or subcutaneous LMWH after 12-24h of delivery.
(VTE 2-4 wks EDD)	● Initiate therapy with IV heparin to achieve therapeutic level; switch to SC heparin. ● Discontinue SC 24h prior to procedure & initiate IV heparin. ● Discontinue IV heparin 6h before procedure & restart 6h after procedure.
<2 wks	● Place IVC filter ● Initiate IV UFH ● Discontinue UFH 6hrs before procedure & restart after 6hrs of procedure.

	Prophylatic	Therapeutic
UFH	● 5000 U SC BD – 1st trimester ● 7500 U SC BD – 2nd trimester ● 10,000 U SC BD – 3rd trimester	Total daily requirement of IV heparin divided into twice daily dosing.
LMWH	● Standard dose < 20wks ● Double dose >20 wks	Standard therapeutic dose , titrate to anti Xa level.

Duration of therapy

Anticoagulation treatment is continued for atleast 6 weeks postpartum and for a minimum of 3 months.

Updated on 9/3/2024

Reference

Tintinalli

Peripartum pulmonary embolism : By margeret ;chest med